Case Report: Edema related to olanzapine therapy

Dorian Deshauer, MD, FRCP **Louise Erwin,** RN **Jamie Karagianis,** MD, FRCPC

Family physicians are often the first to hear from their patients about adverse effects of medication, and understanding the range of these effects can be critical in making long-term treatment decisions. This is particularly relevant for the atypical antipsychotic olanzapine. Weight gain and elevated lipid and glucose levels are associated with atypical antipsychotics. Medication-related edema, a less common side effect, can present unique diagnostic and management challenges. We report on a case of recurrent peripheral edema developing in conjunction with olanzapine treatment, effectively managed with a diuretic for 5 months. Our patient is treated in a multidisciplinary setting, involving a family physician, a psychiatric nurse, and a psychiatrist consultant.

A MEDLINE search from January 1995 to March 2005, using the key words "olanzapine" and "edema," yielded 2 relevant case reports and a case series.[1-3] Contact with the manufacturer yielded an additional report.[4] Premarketing trials estimated the incidence of olanzapine-related edema at 2% to 3%, although confounding factors were present. Among atypical antipsychotics, edema has also been reported in conjunction with risperidone[5] and is mentioned in the product monograph for quetiapine.[6]

Case description

A 50-year-old registered nurse with a history of frequently recurring depression, diagnosed with bipolar disorder type II according to the *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition, was prescribed 2.5 mg of olanzapine. Other medications included citalopram (20 mg daily) and trazodone (50 mg at bedtime). She had a remote history of transient edema of unknown origin, no cardiac or other serious medical conditions, and no history of weight problems. Two days after starting olanzapine therapy, she reported bilateral swelling in her hands and ankles. Edema was verified by her family physician. Results of chest x-ray examination, cardiography, complete blood count, electrolyte and thyroid-stimulating hormone measurements, and liver-function tests were normal.

The edema was successfully managed with furosemide, 20 mg daily. She continued to take 2.5 mg of olanzapine, together with 20 mg of furosemide, for 5 months and showed substantial improvement in her mood and complete resolution of the edema. After 5 months, furosemide was discontinued and the edema recurred. Olanzapine was then discontinued; the edema resolved. Subsequently, however, recurrent depression and mood swings worsened. She had already tried quetiapine, risperidone, divalproex, and lamotrigine, all with less perceived benefit than olanzapine. A repeat challenge with 2.5 mg of olanzapine resulted in edema within 5 days, again successfully treated with furosemide. Because mood instability was not well managed with this dose, olanzapine was increased to 5 mg daily. At this dose, bipedal edema worsened, with pitting to the midshin.

Results of repeated chest x-ray examination, complete blood count, thyroid-stimulating hormone measurement, and liver function tests were normal. Although the edema resolved with 60 mg of furosemide, olanzapine was discontinued, as the patient did not want to continue diuretic treatment long-term. The edema resolved spontaneously within a week of stopping olanzapine and has not required further diuretic treatment.

Discussion

In this case, a pre-existing tendency to develop edema was exacerbated by olanzapine. This exacerbation was dose related, but it was managed effectively with a diuretic. There are reports of peripheral edema associated with trazodone[7] and citalopram[8]; however, the recurrence of edema during olanzapine rechallenge suggests that olanzapine, and not trazodone or citalopram, was the responsible agent. A plausible mechanism remains unknown. As olanzapine is being prescribed for an increasing range of emotional problems, often in combination with other medications, edema related to olanzapine might become more common in general medicine. In our case, managing the edema with a diuretic had to be weighed against discontinuing the olanzapine. The decision process involved the patient, her husband, and the multidisciplinary team. After considering the alternatives, we decided that discontinuing olanzapine, coupled with more attention to lifestyle modification, was the best choice. In the future, if

Dr Deshauer *is a psychiatrist and* **Ms Erwin** *is a community mental health nurse at the Royal Ottawa Hospital in Ontario.* **Dr Karagianis** *is Associate Vice President of Clinical Research for Eli Lilly Canada Inc in Toronto, Ont, and is Adjunct Professor of Psychiatry at Memorial University of Newfoundland in St John's.*

This article has been peer reviewed.
Cet article a fait l'objet d'une révision par des pairs.
Can Fam Physician 2006;52:620–621.

EDITOR'S KEY POINTS

- This case highlights edema, a fairly uncommon (2% to 3% incidence) side effect of olanzapine therapy. This edema was independent of weight gain, and there were no signs of congestive heart failure or other medical problems.
- The edema was successfully managed with furosemide, although no data show whether this approach is safe in the long-term.

POINTS DE REPÈRE DU RÉDACTEUR

- L'œdème décrit dans cet article est un effet indésirable relativement rare (incidence de 2% à 3%) du traitement à l'olanzapine. Il n'était pas associé à une prise de poids ni à des signes d'insuffisance cardiaque ou d'autres problèmes médicaux.
- L'administration de furosémide a fait disparaître l'œdème; il n'existe toutefois pas de données concernant l'innocuité à long terme d'un tel traitement.

her condition warrants it, our patient would still consider a brief course of olanzapine, and she felt relieved to know the edema was a self-limited adverse effect.

Conclusion

While olanzapine-related edema can be reversed with a diuretic, little is known about the long-term efficacy or safety of this intervention. Given the increased use of atypical antipsychotic medications in the acute phases of recurrent mood disorders, physicians treating patients in the maintenance phases will be called on to recognize and manage a range of side effects including medication-related edema. For some patients, psychiatric medications added during acute clinical recurrences can be safely reduced or stopped during the maintenance phase.

Correspondence to: **Dr Dorian Deshauer,** *Mood Disorder Clinic, Bipolar Clinical Research Unit, Royal Ottawa Hospital, 1145 Carling Ave, Perley Bldg 2, Ottawa, ON K1Z 7K4; telephone 613 722-6521, extension 6259; fax 613 798-2993; e-mail* **deshauer1@sympatico.ca**

References

1. Yovtcheva SP, Yazel JJ. Olanzapine-induced bilateral pedal edema: a case report. *Gen Hosp Psychiatry* 2000;22:290-1.
2. Ng B, Postlethwaite A, Rollnik J. Peripheral oedema in patients taking olanzapine. *Int Clin Psychopharmacol* 2003;18:57-9.
3. Christensen RC. Olanzapine-associated bilateral pedal edema. *J Clin Psychiatry* 2003;64:972.
4. Farooque R. Uncommon side effects associated with olanzapine. A case report. *Pharmacopsychiatry* 2003;36:83.
5. Ravasia S. Risperidone-induced edema. *Can J Psychiatry* 2001;46:453-4.
6. AstraZeneca. Seroquel. In: Repchinsky C, Editor-in-Chief. *Compendium of pharmaceuticals and specialties. The Canadian drug reference for health professionals.* Ottawa, Ont: Canadian Pharmacists Association; 2004. p. 1851-4.
7. Barrett J, Frances A, Kocsis J, Brown R, Mann JJ. Peripheral edema associated with trazodone: a report of ten cases. *J Clin Psychopharmacol* 1985;5:161-4.
8. Lunbeck. Celexa. In: Repchinsky C, Editor-in-Chief. *Compendium of pharmaceuticals and specialties. The Canadian drug reference for health professionals.* Ottawa, Ont: Canadian Pharmacists Association; 2004. p. 386-9.